

XXV-2. The Kidney and Ureter

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A multiplicity of tumors of renal origin may occur (see Table, p. 1666). However, only the major types found in adults will be considered here. The most important renal tumors of adulthood are those arising from the renal parenchyma, and those arising from the urothelium of the renal pelvis. The important tumors found in infants and children are Wilms' tumors or nephroblastomas (see XXXII-1). Hamartomas constitute another group that must be considered in differential diagnosis, but they are not usually life-threatening.

Renal Cell Carcinoma (Hypernephroma)

These tumors have been known to exist for centuries, but specific attention was drawn to them in the nineteenth century when Grawitz named them hypernephromas,¹² because it had been previously proposed that they arose from adrenal rests. It took 25 years to dispel this conjecture, but we still use the term in everyday parlance. The site of origin is probably the tubular cells, since it has been shown that renal cell carcinomas react positively with fluorescein-labeled anti-human kidney serum.²⁷ Most of the fluorescence is found in the normal tubular epithelium, as well as in the neoplastic areas. In renal cell cancer, absorption of the kidney-specific antiserum results in continued fluorescence of the renal tubule and, of course, loss of fluorescence of the neoplastic tissue. These experiments suggest that the renal tubular cell is the source of renal cell carcinoma, and that there is antigenic loss in these neoplasms. They do not answer any questions concerning gain of

antigen or change in determinants by the tumor, however.

These tumors are relatively uncommon. The American Cancer Society estimated that 6800 Americans would die of renal cell carcinoma in 1973.¹ There is a constant ratio of 2:1 for men and women. About 1% occur in the first decade of life, the greatest incidence being in the sixth decade, with a rapid decrease after that time.

The causative agents in man are unknown, but there are extensive data on experimental and naturally occurring tumors in many different species. No attempt will be made to include here all the information available.

The Leopard frog, *Rana pipiens*, is infected with a viral agent that produces renal adenocarcinomas with great frequency.¹⁸ The populations found about lakes in Vermont, Minnesota, and Michigan demonstrate high incidences of adenocarcinoma, while spontaneously occurring tumors are not encountered in frogs found in Louisiana and North Dakota. Interestingly, the frogs from these latter areas develop tumors when held at tumor-promoting conditions.²⁰

Cats, dogs, and other domestic animals develop lethal renal adenocarcinomas that are presumably spontaneous.²⁴ The use of dietary lead and irradiation in rats produces adenomas and occasionally tumors that metastasize. The administration of dimethylnitrosamine to newborn or adult rats will produce adenocarcinomas that are lethal,³⁷ though this compound produces hepatic toxicity and hepatic neoplasia as well. Among the more predictable carcinogens is aflatoxin B₁,⁹ which produces renal neoplasms in over half the rats to whom it is fed.

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Exhibit G

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ter, J., and Harrison,
extraadrenal pheochro-
mod sampling. Surg.

use with tumor of
J. VMA, 27:1047.

cytological effects of
n. J. Nat. 1395.
Royal Coll. Surg.

d hypertension asso-
Assoc. Amer. Phys.

ers, W., and Selama,
a. Cushing's disease.

tionian, G. S., and
cally treated adreno-
3:25, 1950.

The hormones of the
n. J. Nat. 1943.

n, L., Robertson, A.,
erative malignancy
J. Brit. Med. J., 1951.

in, A., Neher, E., Von
dler, O. Kriminologi-
fionds, Experimenta.

adrenal. S. Blockade
synthesis by alpha-
tyrosine hydroxylase.
1962.

: Radiotherapy and
J. A. 205:159, 1968.

iscarello, M. G., and
g. following bilateral
with advanced hyper-
Assoc. Amer. Phys.

nd Tins, J. C. Focal
chromocytoma. New

the sympathomimetic
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card. J. Nat. 1948.
cretion of noradrenaline-
chromocytoma. Ann.

resent status of diag-
noma. Circulation.

embryology, sym-
toma and radiation
6:405, 1941.

ies, Hemaphysoma
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Renal neoplasms also have been produced in male Syrian Golden hamsters by the administration of stilbestrol.¹¹ Female hamsters did not develop tumors, nor did castrated males, and testosterone prevented the growth of transplanted tumors. Based on these observations, which indicated that in this experimental model alteration in hormonal milieu changed the growth characteristics of the tumors under evaluation, patients were treated with testosterone and progesterone (Provera).⁵ Regression of metastases occurred in four of twenty patients (see XIV-7).

In man, there is no incisive evidence that any carcinogen produces renal carcinoma, but there is a suggestion from epidemiologic data that both adenoma and adenocarcinoma are increased in smokers²; patients with diabetes also may be at higher risk.³⁹

Pathology

The only satisfactory term for this tumor is "renal adenocarcinoma"; there is no virtue in continuing to labor with inappropriate names like "hypernephroma" or "Grawitz's tumor." They arise from tubular epithelium, and their histology is diverse, not only from tumor to tumor, where it is exceedingly so, but often within the same neoplasm. The tumors may be separated into two broad groups, clear cell tumors and granular cell tumors (Fig. XXV-2-1, A and

B). Imprecision is inherent in this and other classifications, since these two cell types occur together. It is held by some that tumors with predominantly clear cells carry a somewhat better prognosis than do those with granular cells.^{10,25} Others have failed to confirm this.¹⁵ In a recent review,⁹ it was clearly demonstrated that three closely related features are critical in assessing prognosis: the general histologic structure of the tumor, the presence of capsular invasion, and infiltration of the renal veins.^{7,13} Renal venous invasion may prove to be not so critical a finding when present alone, since it was found to be a serious sign only when other extensions were also present.³⁵ Further, the material for analysis in most studies is not uniformly good, and the exact definition of renal vein involvement is not given often; therefore, room for interpretation exists here. Certainly, extension outside the kidney capsule and the presence of nodal metastases are associated with a marked decrease in survival.

Metastases occur by way of venous and lymphatic spread, as well as by direct extension to contiguous structures. The lungs, bones, and liver are the most frequent sites involved, and though the impression is that solitary metastatic lesions are seen with relative frequency, they are actually uncommon.

Confusion persists concerning one matter often re-examined: the relationship of renal

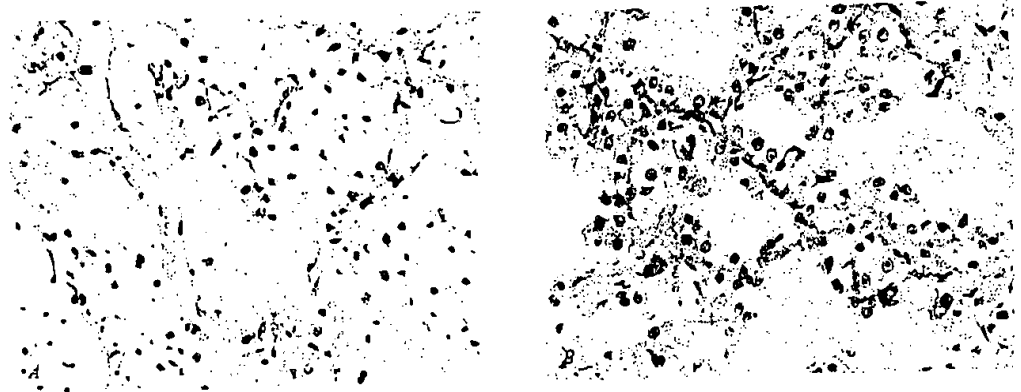


FIG. XXV-2-1. A and B, Clear cell and granular renal cell carcinoma. $\times 320$.